

WHAT IS CLAIMED IS:

1. An isolated nucleic acid encoding an osteoprotegerin binding protein selected from the group
5 consisting of:

a) the nucleic acid sequence as in Figure 1 (SEQ ID NO: 1) and Figure 4 (SEQ ID NO: 3);

b) nucleic acids which hybridize to the polypeptide coding regions as shown in Figure 1 (SEQ ID
10 NO: 1) and Figure 4 (SEQ ID NO: 3) and remain hybridized under high stringency conditions; and

c) nucleic acids which are degenerate to the nucleic acids of (a) or (b).

15 2. The nucleic acid of Claim 1 which is cDNA, genomic DNA, synthetic DNA or RNA.

3. A polypeptide encoded by the nucleic acid of Claim 1.
20

4. The nucleic acid of Claim 1 including one or more codons preferred for Escherichia coli expression.

25 5. The nucleic acid of Claim 1 having a detectable label attached thereto.

6. A nucleic acid encoding a polypeptide comprising the amino acid sequence of residues 1-316
30 and residues 70-316 as shown in Figure 1 (SEQ ID NO: 1).

7. residues 1-316 as shown in Figure 4 (SEQ ID NO: 3);

8. A nucleic acid encoding a soluble osteoprotegerin binding protein.

5 9. The nucleic acid of Claim 8[✓] encoding a polypeptide comprising residues 69-317 as shown in Figure 4 (SEQ ID NO: 3) and truncations thereof;

10 10. An expression vector comprising the nucleic acid of Claims 1 and 9.

11. The expression vector of Claim 10 wherein the nucleic acid comprises the polypeptide-encoding region as shown in Figure 1 (SEQ ID NO: 1) and Figure 4 (SEQ ID NO: 3);

15

12. A host cell transformed or transfected with the expression vector of Claim 10.

13. The host cell of Claim 12 which is a eucaryotic or procaryotic cell.

20

14. The host cell of Claim 13 which is Escherichia coli.

15 15. A process for the production of an osteoprotegerin binding protein comprising:

growing under suitable nutrient conditions host cells transformed or transfected with the nucleic acid of Claim 1; and

30 isolating the polypeptide product of the expression of the nucleic acid.

17. A purified and isolated osteoprotegerin binding protein, or fragment, analog, or derivative thereof.

5 18. The protein of Claim 17 which is a human osteoprotegerin.

10 19. The protein of Claim 17 having the amino acid sequence as shown in Figure 1 (SEQ ID NO: 2) and Figure 4 (SEQ ID NO: 4).

20. The protein of Claim 17 which has been covalently modified with a water-soluble polymer.

15 21. The protein of Claim 20 wherein the polymer is polyethylene glycol.

20 22. The protein of Claim 17 which is a soluble osteoprotegerin binding protein.

23. The protein of Claim 22 comprising the amino acid sequence from residues 70-316 inclusive as shown in Figure 1 (SEQ ID NO: 2), or a fragment, analog, or derivative thereof.

25 24. The protein of Claim 22 comprising the amino acid sequence from residues 69-317 inclusive as shown in Figure 4 (SEQ ID NO: 4) and truncations thereof.

30 25. An antibody or fragment thereof which

monoclonal antibody.

27. A method for detecting the presence of an osteoprotegerin binding protein in a biological sample comprising:

5 incubating the sample with the antibody of Claim 25 under conditions that allow binding of the antibody to the osteoprotegerin binding protein; and detecting the bound antibody.

28. A method for detecting the presence of osteoprotegerin in a biological sample comprising:

10 incubating the sample with an osteoprotegerin binding protein under conditions that allow binding of the protein to osteoprotegerin; and measuring the bound osteoprotegerin binding
15 protein.

29. A method to assess the ability of a candidate compound to bind to an osteoprotegerin binding protein comprising:

20 incubating the osteoprotegerin binding protein with the candidate compound under conditions that allow binding; and measuring the bound compound.

25 30. The method of Claim 29 wherein the compound is an agonist or an antagonist of an osteoprotegerin binding protein.

30 31. A method of regulating expression of an osteoprotegerin binding protein in an animal comprising administering to the animal a nucleic acid

32. A pharmaceutical composition comprising a therapeutically effective amount of an osteoprotegerin

binding protein in a pharmaceutically acceptable carrier, adjuvant, solubilizer, stabilizer and/or anti-oxidant.

5 33. The composition of Claim 32 wherein the osteoprotegerin binding protein is a human osteoprotegerin binding protein.

10 34. A method of preventing or treating bone disease in a mammal comprising administering a therapeutically effective amount of a modulator of an osteoprotegerin binding protein.

15 35. The method of Claim 34 wherein the modulator is a soluble form of an osteoprotegerin binding protein.

20 36. The method of Claim 35 wherein the modulator is an antibody, or fragment thereof, which specifically binds an osteoprotegerin binding protein.

25 37. The protein of Claim 22 comprising the amino acid sequence from residues 140-316 inclusive as shown in Figure 4 (SEQ ID NO. 4) or a fragment, analog or derivative thereof.

30 38. The protein of Claim 22 comprising the amino acid sequence from residues 145-316 inclusive as shown in Figure 4 (SEQ ID NO. 4) or a fragment, analog or derivative thereof.

35 osteoclast differentiation and activation receptor.

40. The method of Claim 39 wherein the modulator is a soluble form of an osteoclast differentiation and activation receptor.

5 41. The method of Claim 39 wherein the modulator is an antibody, or fragment thereof, which specifically binds an osteoclast differentiation and activation factor.

10 42. A method to assess the ability of a test compound to increase or decrease binding of osteoprotegerin binding protein to ODAR comprising:

15 incubating osteoprotegerin binding protein, ODAR and optionally the test compound under conditions that allow binding of osteoprotegerin binding protein to ODAR; and

 measuring the binding of osteoprotegerin binding protein to ODAR in the absence and presence of the test compound.

20